results confirm previously published forensic evidence demonstrating that EVs could be significantly associated with sudden cardiac unexpected death cases (2). Evidently, it has been previously established that these EV cardiotropic strains did not respect national borders (2–5).

In this study (1), the endomyocardial detection of viral capsid protein 1 (VP1) by immunohistochemical technique was found to be the best tool for the diagnosis of EV-associated heart diseases as previously described (4,5), and no heart tissue control samples were VP1 positive using our improved immunohistological protocols (6). The VP1 results were confirmed by molecular assays and in some cases by the use, after cloning, of nucleic acid sequencing of the VP1 region (1). Moreover, none of the 20 EV-positive patients with acute MI and none of the 2 EV-positive subjects from the healthy heart control group were positive for the detection of other cardiotropic viruses, including Epstein-Barr virus, herpes simplex viruses, cytomegalovirus, varicella-zoster virus, adenoviruses, and parvovirus B19, in their myocardial tissues using previously published polymerase chain reaction techniques (1). However, 60% of the EV-negative heart tissues of MI patients were positive for the molecular detection of 1 or several of these cardiotropic viruses, including parvovirus B19 (not shown). These results support the previous published data on the potential role of myocardial virus persistence in differential aspects of endothelial function of the coronary microcirculation endothelial activation, and myocardial leukocyte infiltrates (7–9). By consequence, the role of other cardiotropic viruses including parvovirus B19-persistent infection in the development of coronary diseases remains to be explored, and it, therefore, is possible that other viruses may be associated to EV cardiovascular infections and may trigger the inflammatory process of chronic arteriosclerosis leading to acute MI (7).

Finally, there is no evidence of a new element of the "French paradox" related to the way of life including wine drinking, and which may concern a specific cardiovascular protection against common cardiotropic viruses (8). However, the French red wine is better than German beer for our arteries, but this drink remains to be consumed with moderation (10).

***Laurent Andréoletti, MD, PhD**

*Laboratoire de Virologie
Service de Microbiologie
Hôpital Robert Debré
et faculté de médecine de Reims
Avenue du Général Koenig
51092 REIMS Cedex
France
E-mail: landreoletti@chu-reims.fr

doi:10.1016/j.jacc.2008.03.035

REFERENCES

1. Andréoletti L, Ventéo L, Douche-Aourik F, et al. Active coxsackieviral B infection is associated with disruption of dystrophin in endomyocardial tissue of patients who died suddenly of acute myocardial infarction. J Am Coll Cardiol 2007;50:2207–14.
2. Cioc AM, Nuovo GJ. Histologic and in situ viral findings in the myocardium in cases of sudden, unexpected death. Mod Pathol 2002;9:914–22.
3. Yilmaz A, Mahrholdt H, Athanasiadis A, et al. Coronary vasospasm as the underlying cause for chest pain in patients with PVB19-myocarditis. Heart 2008 Jan 29;[Epub ahead of print].
4. Andréoletti L, Bourlet T, Moukassa D, et al. Enteroviruses can persist with or without active viral replication in cardiac tissue of patients with end-stage ischemic or dilated cardiomyopathy. J Infect Dis 2000;182:1222–7.
5. Li Y, Bourlet T, Andréoletti L, et al. Enteroviral capsid protein VP1 is present in myocardial tissues from some patients with myocarditis or dilated cardiomyopathy. Circulation 2000;101:231–4.
6. Zhang H, Li Y, Peng T, et al. Localization of enteroviral antigen in myocardium and other tissues from patients with heart muscle disease by an improved immunohistochemical technique. J Histochem Cytochem 2000;48:5798.
7. Vallbracht KB, Schwimmbeck PL, Kuhl U, Seeberg B, Schultheiss HP. Endothelium dependent flow-mediated vasodilation of systemic arteries is impaired in patients with myocardial virus persistence. Circulation 2004;110:2938–45.
8. Vallbracht KB, Schwimmbeck PL, Kuhl U, Rauch U, Seeberg B, Schultheiss HP. Differential aspects of endothelial function of the coronary microcirculation considering myocardial virus persistence, endothelial activation, and myocardial leukocyte infiltrates. Circulation 2005;111:1784–91.
9. Kuhl U, Pauschinger M, Bock T, et al. Parvovirus B19 infection mimicking acute myocardial infarction. Circulation 2003;108:945–50.
10. Renaud S, de Lorgeril M. Wine, alcohol, platelets, and the French paradox for coronary heart disease. Lancet 1992;339:1523–6.

The Challenges of Cardiovascular Research in Developing Countries

We read with interest the recent article by Prabhakaran et al. (1) reporting the results of the Global Cardiovascular Disease Research Survey. Not surprisingly, the study shows a low research output in developing (low-income and low-middle-income) countries. The authors postulate that a major reason for this low output is low government spending, and they recommend that governments in these countries increase their research funding to improve research output.

The issues related to research and funding in developing countries are complicated and multifactorial. It is easy to say that increasing research funding in these countries will improve their productivity, and this is probably true. Yet, the implementation of this recommendation is difficult. It is very difficult to convince governments in developing countries, with limited financial resources, to invest in research when a significant percentage of their populations still does not have water and electricity supplies. Similarly, it is very difficult for universities and hospitals to invest in research when their financial resources can barely fulfill their basic requirements in medical care and medical education.

Furthermore, although funding is certainly an essential component in the advancement of research, it is not the only one. Another very important component, which is not easy to study and analyze, is human resources. Performing high-quality research requires the recruitment of established senior investigators who can enhance research productivity and, more importantly, train young junior investigators to sustain research activity. These high-quality investigators require not only funding but also political, economic, and social stability. The U.S. and Europe have thousands of investigators who originally came from developing countries. These scientists reside in the U.S. and Europe not only because of the availability of funds but also because of political, economic, and social stability that they do not have in their home countries.

With all of these limitations, does this mean that developing countries should forget about medical research? No, but they should have realistic expectations and rational policies that can guide the utilization of their very limited resources. These policies should probably focus research funding on selective centers with selected high-quality investigators who can use these resources to produce high-quality research. It is also very important to encourage collaboration with investigators and institutions in developed countries. We have recently analyzed the research productivity of the medical faculty in our institution (2) and found that collaboration with investigators in developed countries significantly improved the quality of our medical center's research output.

Cardiovascular research is essential for the advancement of human health. The study by Prabhakaran et al. (1) indicates that developing countries have not yet made significant contributions in this field, in spite of the fact that their populations carry a major percentage of the global burden of cardiovascular diseases. The problem is clear. The solutions, however, are very difficult.

***Habib A. Dakik, MD, FACC**

*Associate Professor of Medicine
American University of Beirut
P.O. Box 11-0236/A38
Beirut
Lebanon
E-mail: hd01@aub.edu.lb

doi:10.1016/j.jacc.2008.02.079

REFERENCES

1. Prabhakaran P, Ajay VS, Prabhakaran D, et al. Global cardiovascular disease research survey. J Am Coll Cardiol 2007;50:2322.
2. Dakik HA, Kaidbey H, Sabra R. Research productivity of the medical faculty at the American University of Beirut. Postgrad Med J 2006;82:462–4.

Reply

We thank Dr. Dakik for his interest in and comments on our article (1). We largely agree with his observations about the multifactorial determinants of the low research output related to cardiovascular disease (CVD) research in low-income and low-middle-income countries. We do, however, differ with some perspectives. For example, Dr. Dakik argues that collaboration with investigators in developed countries raises the quality of published articles. Although this is true to some extent, it hampers local capacity enhancement and original research from developing-country scientists, as in most such publications, the corresponding authors are from the developed country (data not shown). Further, there are hardly any collaborative studies aimed at improving health systems, quality of care, and translational research. Collaboration with developed-country investigators, in the absence of national funding, compels developing-country investigators to accept research agendas set by their funding partners. Availability of national funding for research enables a greater balance to be attained in research undertaken by developing-country investigators. The aim of our article was to raise awareness of the low priority afforded to CVD and to argue for enhanced allocation of resources to CVD prevention and control.

In addition, there is a lack of information on how the estimated $2.4 billion spent by low- and middle-income countries in health research and development in 2003 (2) was allocated across different disease or disciplinary categories. Although anecdotal information from these countries suggests that public-sector spending on CVD-related research is limited, this question needs further systematic quantification.

Although we need to further study the issues raised by Dr. Dakik, as well as other determinants of the volume and variety of CVD-related research, we cannot ignore the advancing epidemic of CVD in developing countries. Therefore, governments need to spend at least a small portion of their funds on translational and operational research for enhancing the provision of inexpensive, effective, and evidence-based care for established CVD and to develop cost-effective strategies aimed at health promotion for primary prevention of CVD.

Poornima Prabhakaran, MBBS, Dip Epidemiol
Vamadevan S. Ajay, MPH
Dorairaj Prabhakaran, MD, DM, MSc
***Kolli Srinath Reddy, MD, DM, MSc**

*Vice-Chair
Initiative for Cardiovascular Health Research in the Developing Countries (IC-HEALTH)
C-1/52, 2nd Floor
Safdarjung Development Area
New Delhi 110 016
India
E-mail: ksreddy@ichealth.org

doi:10.1016/j.jacc.2008.03.038

REFERENCES

1. Prabhakaran P, Ajay VS, Prabhakaran D, et al. Global cardiovascular disease research survey. J Am Coll Cardiol 2007;50:2322.
2. Global Forum for Health Research. Monitoring Financial Flows for Health Research 2006. Geneva: Global Forum for Health Research, 2006. Available at: http://www.globalforumhealth.org/filesupld/monitoring_financial_flows_06/Financial%20Flows%202006.pdf. Accessed October 8, 2007.